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Research Article

Study the Role of Combined M2-Pyruvate Kinase, Calprotectin and Occult Blood Test as Fecal Biomarkers for Early Detection of Colorectal Cancer

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Abstract

Background and Study Aim: One of the main requirements of biomarkers for detecting CRC is that it must allow detection of the disease at earlier stages. The current study is designed to investigate the role of combined M2-Pyruvate kinase, Calprotectin, and Fecal occult blood test measurements as fecal diagnostic biomarkers for early detection of colorectal cancer.

Patients and Methods: Total number of 72 subjects (48 patients and 24 healthy controls) were included in the study. Patients with cancer colon and patients with organic non-malignant colorectal lesions were recruited from Oncology and Gastroenterology Outpatient Clinics and Inpatient Department Menoufia University Hospital.

Results: There was a highly significant difference between studied groups regarding age and gender (P> 0.001), cancer colon was higher among old age (mean ± SD is 58.96 ± 6.3) and males (70.8%), There was a highly significant difference between studied groups regarding Hb, CRP and ESR (P >0.001); lowest Hb level was detected in cancer group (8.7 ± 1.7). On the other hands highest CRP and ESR levels were in cancer group (7.29 ± 4.47) and (14.71 ± 6.19) respectively. There was a significant difference between studied groups regarding platelets (P >0.05); lowest platelet number was detected in cancer group (272.4 ± 66.9). There was non-significant difference between studied groups regarding WBCs (P <0.05); highest WBCs number was detected in cancer group (8.05 ± 2.3), There was a highly significant difference between studied groups regarding colonoscopy (P >0.001), There was a highly significant difference between studied groups regarding M2-Pyruvate kinase and Occult Blood (P >0.001), There was highly significant difference between M2-PK in cancer and control groups (p >0.001), There was significant difference between calprotectin in cancer and control groups (p >0.05), There was highly significant difference between occult blood in cancer and control groups (p >0.001), There was highly significant difference between Combined M2-PK and Calprotectin in cancer and control groups (p >0.001), There was highly significant difference between Combined M2-PK and Occult blood in cancer and control groups (p>0.001), There was highly significant difference between Combined M2-PK, Calprotectin and occult blood in cancer and control groups (p >0.001).

Conclusion: Our study confirms that, Colorectal Cancer (CRC) increases with age and it is more common in male, CRP and ESR increase in CRC patients, Fecal M2PK, FC and FOBT in stool increase significantly in CRC patients, Sensitivity, specificity and accuracy of screening for CRC are highest in combination of fecal M2PK, occult blood in stool and FC tests.

Keywords: Colorectal Cancer; M2-Pyruvate Kinase; Calprotectin

Introduction

Colorectal cancer (CRC) could be a quite common and infrequently fatal cancer within the U.S. and worldwide. Screening has been shown to be extremely effective in preventing the incidence and ensuant mortality from CRC. For this reason, within the U.S., CRC screening has been supported by all major medical societies, receiving a Grade-A recommendation by the United States Preventive Services Task Force (USPSTF) in its most recent tips.

Colorectal cancer morbidity and mortality rates also are affected by complications arising from body part surgery. Up to thirty fifth of body part surgery patients suffer from postoperative complications, which are shown to translate to a worse quality of life, poor oncological outcomes, extra complications, and overall higher risk for mortality.

Pyruvate enzyme (PK, EC: 2.7.1.40) could be an extremely regulated glycolytic catalyst found all told living organisms This catalyst catalysis the last step of metastasis and mediates the transferring of a phosphate cluster from phosphoenolpyruvate (PEP) to nucleoside diphosphate (ADP) to supply acid and ATP (ATP). PK has four totally different isoenzymes, that primarily depends upon the metabolic response of various cells and tissues. each L and M genes write in code PK isoenzymes.

Several biomarkers are tested, since the multistep process from benign tumor to colon malignant neoplastic disease has been established, together with dirty occult blood, determination of pyruvate enzyme isoform M2 (M2-PK), and endocannabinoid system molecules. M2-PK is gift primarily within the dimeric kind and isn't associated among the glycolytic catalyst complicated. Consequently, in these cells, the (ATP +GTP): (CTP +UTP) quantitative relation is low. The stable expression of induces AN inhibition of cell proliferation on the one hand. However, on the opposite hand, resolutely prepares the metabolome of the cells for transformation by dramatically boosting metabolism.

Fecal calprotectin (FC) could be a reliable surrogate marker of gut inflammation throughout the canal and is useful for discriminating between organic and non-organic gut disease. FC could be a calcium-binding macromolecule that's mostly con fined to the cytoplasm of white blood corpuscle granulocytes and macrophages; Item is extraordinarily stable within the feces and is free in biological fluids underneath inflammatory conditions.

Patients and Methods

Type of study is Case control, retrospective and analytic study.

Patient selection: Total number of 72 subjects (48 patients and 24 healthy controls) were included in the study. Patients with cancer colon and patients with organic non-malignant colorectal lesions were recruited from Oncology and Gastroenterology Outpatient Clinics and Inpatient Department Menoufiya University Hospital.

Informed consents were obtained from all patients included in the study which approved by the local ethics committee of Faculty of Medicine, Menoufia University.

Patients were classified into three equal groups:

- Group I: Included 24 patients with cancer colon.
- Group II: Included 24 patients with organic non-malignant colorectal lesions.
- Group III: Included 24 healthy volunteers as a control group.

All patients and control group were subjected to the following:

1. Through history taking.
2. Clinical examination (general and local).
3. Laboratory investigations including:
    - Complete blood count (CBC).
    - Liver function tests.
    - Viral marker: HBs Ag and Hcv Ab by ELISA.
    - Renal function tests.
    - Erythrocyte Sedimentation Rate (ESR).
    - C-reactive protein (CRP).
4. Radiology
5. Sigmoidoscopy and complete colonoscopy when is indicated.
6. Histopathological examination of colonic biopsy.
7. The 3 fecal non-invasive biomarkers:
    - M2-PK: (5 to 100 units/ml (U/ml) EDTA-plasma)
    - Calprotectin 50+200: (A:50 and B:200)
    - Fecal Occult Blood Test (FOBT): (positive or negative).

Statistical analysis

Descriptive statistics: Qualitative data was expressed in: Number (No) and percentage (%), while quantitative data was expressed in: mean ($\bar{x}$) and standard deviation (SD).

Analytic statistics

- Chi square test (X2): Was used to study association between two qualitative variables. Whenever any of the expected cells were less than five, Fischer's Exact test was used.
- ANOVA test: Was used for comparison of quantitative variables between more than two groups of normally distributed data with LSD test as post Hoc test.
- Kruskal Wallis test: Was used for comparison of quantitative variables between more than two groups of not normal distributed data with Tamhane's test as post hoc test.
- Sensitivity is the proportion of patients with disease who test positive = TP/(TP+FN).
- Specificity is the proportion of patients without disease who test negative = TN/(TN + FP).
- Predictive value of a positive test (PPV) is the proportion of patients with positive tests who have disease = TP/(TP+FP).
- Predictive value of a negative test (NPV) is the proportion of patients with negative tests who do not have disease = TN/(TN+FN).
- P value:
- P value of > 0.05 was considered statistically non-significant.
- P value of < 0.05 was considered statistically significant.
- P value of < 0.001 was considered statistically highly significant.

Results

Socio-demographic data	Control group (n = 24) N (%)	Cancer colon group (n = 24) N (%)	Pre-cancerous group (n = 24) N (%)	Total (n = 72) N (%)	Test of significance	P value
Age: Mean ± SD Range (min.-max.)	 45.3±10.6 35-18	 58.96±6.3 52-72	 41.1±10.6 24-61	 48.4±12.03 24-81	ANOVA = 23.796	>0.001** Post Hoc test (LSD): P1= >0.001** P2= 0.125 P3= >0.001**
Gender: Male Female	 8 (33.3) 16 (66.7)	 17 (70.8) 7 (29.2)	 22 (91.7) 2 (8.3)	 47 (65.3) 25 (34.7)	X^2= 18.506	>0.001**
Complaint: Chronic diarrhea Chronic abdominal pain Diarrhea and abdominal pain Chronic irritable bowel Bleeding per rectum Weight loss and bleeding Anemia Weight and appetite loss Hematemesis Anemia and abdominal pain	 1 (4.2) 18 (75) 1(4.2) 4 (16.7) 0 (0) 0 (0) 0 (0) 0 (0) 0 (0) 0 (0)	 0 (0) 1 (4.2) 0 (0) 0 (0) 18 (75) 1 (4.2) 1 (4.2) 2 (8.3) 1 (4.2) 0 (0)	 5 (20.8) 12 (50) 0 (0) 0 (0) 6 (25) 0 (0) 0 (0) 0 (0) 0 (0) 1 (4.2)	 6 (8.3) 31 (43.1) 1 (1.4) 4 (5.6) 24 (33.4) 1 (1.4) 1 (1.4) 1 (1.4) 2 (2.8) 1 (1.4)	X^2= 65.205	>0.001**

Table 1: Socio-demographic characteristics of studied groups.

P1: between control group and cancer colon; P2: between control group and pre-cancerous; P3: between cancer colon and pre-cancerous; **P value >0.001: highly significant; ANOVA: analysis of variance; LSD: least significant difference (Post Hoc test); X2: Chi square test.

This table shows that: There was a highly significant difference between studied groups regarding age and gender (P> 0.001), cancer colon was higher among old age (mean ± SD is 58.96 ± 6.3) and males (70.8%).

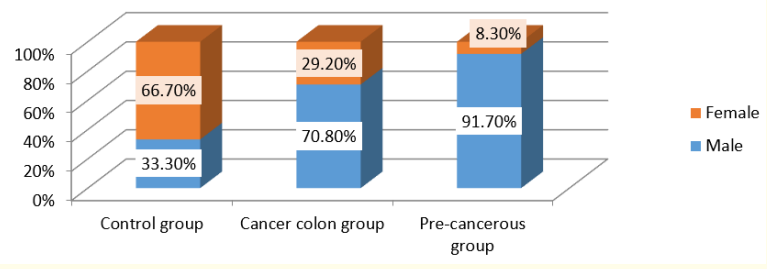

Figure 1: Gender distribution of studied groups.

Lab investigations	Control group (n= 24)	Cancer colon group (n= 24)	Pre-cancerous group (n= 24)	Total (n= 72)	Test of significance	P value
Hb: Mean ± SD Range (min.-max.)	 12.8±0.9 10.7-14.5	 8.7±1.7 5.3-11.4	 12.1±1.9 6.5-14.5	 11.2±2.4 5.5-14.5	ANOVA=45.651	>0.001** Post Hoc test (LSD): P1= >0.001** P2= 0.159 P3= >0.001**
Platelet: Mean ± SD Range (min.-max.)	 288.9±48.3 215-378	 272.4±66.9 197-372	 334.8±76.7 197-525	 298.7±69.4 197-525	ANOVA=5.93	0.004* Post Hoc test (LSD): P1= 0.381 P2= 0.017* P3= 0.001*
WBCs: Mean ± SD Range (min.-max.)	 6.98±1.3 5.3-9.3	 8.05±2.3 4.6-11.9	 7.97±1.97 5.7-11.5	 7.7±1.93 4.6-11.9	ANOVA=2.395	0.099
CRP: Mean ± SD Range (min.-max.)	 2.38±1.53 1-8	 7.29±4.47 2.5-20	 4.31±2.84 1.5-12	 4.66±3.74 1-20	K-W=29.291	>0.001** Post Hoc test (Tamhane): P1= >0.001** P2= 0.017* P3= 0.027*
ESR: Mean ± SD Range (min.-max.)	 6.58±2.48 3-11	 14.71±6.19 8-30	 9.13±5.91 3-30	 10.14±6.12 3-30	K-W=29.845	>0.001** Post Hoc test (Tamhane): P1= >0.001** P2= 0.173 P3= 0.008*

Table 2: Laboratory investigations of studied groups.

P1: between control group and cancer colon; P2: between control group and pre-cancerous;

P3: between cancer colon and pre-cancerous; *P value >0.05: significant; P value <0.05: non-significant; K-W: Kruskal-wallis test.

There was a highly significant difference between studied groups regarding Hb, CRP and ESR (P >0.001); lowest Hb level was detected in cancer group (8.7 ± 1.7). On the other hands highest CRP and ESR levels were in cancer group (7.29 ± 4.47) and (14.71 ± 6.19) respectively. There was a significant difference between studied groups regarding platelets (P >0.05); lowest platelet number was detected in cancer group (272.4 ± 66.9). There was non-significant difference between studied groups regarding WBCs (P <0.05); highest WBCs number was detected in cancer group (8.05 ± 2.3).

Variable	Control group (n= 24) N (%)	Cancer colon group (n= 24) N (%)	Pre-cancerous group (n= 24) N (%)	Total (n= 72) N (%)	Test of significance (X^2)	P value
Colonoscopy:						
Unremarkable	22 (91.7)	0 (0)	0 (0)	22 (30.6)		
Mass	0 (0)	22 (91.7)	0 (0)	22 (30.6)		
Polyp	0 (0)	2 (8.3)	15 (62.5)	17 (23.6)	133.412	>0.001**
Ulcer	0 (0)	0 (0)	9 (37.5)	9 (12.5)		
Non-specific colitis	1 (4.2)	0 (0)	0 (0)	1 (1.4)		
Anal fissure	1 (4.2)	0 (0)	0 (0)	1 (1.4)		

Table 3: Comparison between studied groups regarding colonoscopy.

**Highly significant

This table shows that

There was a highly significant difference between studied groups regarding colonoscopy (P >0.001). Colonoscopy showed that 91.7% of cancer colon lesions were masses, while 62.5% of pre-cancerous colonic lesions were polyps.

Fecal biomarkers	Control group (n= 24) N (%)	Cancer colon group (n= 24) N (%)	Pre-cancerous group (n= 24) N (%)	Total (n= 72) N (%)	Test of significance (X^2)	P value
M2-Pyruvate kinase:						
Negative	23 (95.8)	2 (8.3)	10 (41.7)	35 (48.6)	37.473	>0.001**
Positive	1 (4.2)	22 (91.7)	14 (58.3)	37 (51.4)		
Calprotectin:						
Negative	18 (75)	7 (29.2)	13 (54.2)	38 (52.8)	10.142	0.006*
Positive	6 (25)	17 (70.8)	11 (45.8)	34 (47.2)		
Occult Blood:						
Negative	19 (79.2)	2 (8.3)	5 (20.8)	26 (36.1)	29.739	>0.001**
Positive	5 (20.8)	22 (91.7)	19 (79.2)	46 (63.9)		

Table 4: Comparison between studied groups regarding fecal biomarkers.

**Highly significant *Significant.

There was a highly significant difference between studied groups regarding M2-Pyruvate kinase and Occult Blood (P >0.001). Both positive M2-Pyruvate kinase and Occult Blood were higher in cancer colon group than other groups (91.7%). While there was significant difference between studied groups regarding Calprotectin (P> 0.05). Positive Calprotectin was higher in cancer colon group than other groups (70.8%).

M2-PK results	Cancer colon N (%)	Control N (%)	Total	Test of significance (FE)	P value
+ve	22 (91.7) (TP)	1 (4.2) (FP)	23 (47.9)	36.816	>0.001**
-ve	2 (8.3) (FN)	23 (95.8) (TN)	25 (52.1)		
Total	24 (100)	24 (100)	48 (100)		

Table 5: M2-PK as a predictor of cancer colon in relation to control group.

FE: Fischer exact test; TP: true positive; FN: false negative; FP: false positive; TN: true negative.

There was highly significant difference between M2-PK in cancer and control groups (p >0.001).

Variable	Sensitivity	Specificity	Accuracy	PPV	NPV
M2-PK	92%	96%	94%	96%	94%

Table 6: Validity of M2-PK as a predictor of cancer colon.

PPV: Positive predictive value (Predictive value of a positive test); NPV: Negative predictive value (Predictive value of a negative test).

Calprotectin results	Cancer colon N (%)	Control N (%)	Total	Test of significance (FE)	P value
+ve	17 (70.8) (TP)	6 (25) (FP)	23 (47.9)	10.101	0.003*
-ve	7 (29.2) (FN)	18 (75) (TN)	25 (52.1)		
Total	24 (100)	24 (100)	48 (100)		

Table 7: Calprotectin as a predictor of cancer colon in relation to control group.

There was significant difference between calprotectin in cancer and control groups (p >0.05).

Variable	Sensitivity	Specificity	Accuracy	PPV	NPV
calprotectin	71%	75%	73%	74%	72%

Table 8: Validity of calprotectin as a predictor of cancer colon.

Occult blood results	Cancer colon N (%)	Control N (%)	Total	Test of significance (FE)	P value
+ve	22 (91.7) (TP)	5 (20.8) (FP)	27 (56.25)	24.466	>0.001**
-ve	2 (8.3) (FN)	19 (79.2) (TN)	21 (43.75)		
Total	24 (100)	24 (100)	48 (100)		

Table 9: Occult blood as a predictor of cancer colon in relation to control group.

There was highly significant difference between occult blood in cancer and control groups (p >0.001).

Variable	Sensitivity	Specificity	Accuracy	PPV	NPV
occult blood	92%	79%	85%	81%	90%

Table 10: Validity of occult blood as a predictor of cancer colon.

Combined M2-PK and Calprotectin results	Cancer colon N (%)	Control N (%)	Total	Test of significance (FE)	P value
+ve	24 (100)	6 (25)	30 (62.5)	28.8	>0.001**
-ve	0 (0)	18 (75)	18 (37.5)		
Total	24 (100)	24 (100)	48 (100)		

Table 11: Combined M2-PK and Calprotectin as predictors of cancer colon in relation to control group.

FE: Fischer exact test.

There was highly significant difference between Combined M2-PK and Calprotectin in cancer and control groups (p >0.001).

Variable	Sensitivity	Specificity	Accuracy	PPV	NPV
Combined M2-PK and Calprotectin	100%	75%	88%	80%	100%

Table 12: Validity of Combined M2-PK and Calprotectin as predictors of cancer colon.

PPV: Positive predictive value (Predictive value of a positive test).

NPV: Negative predictive value (Predictive value of a negative test).

Combined M2-PK and Occult blood results	Cancer colon N (%)	Control N (%)	Total	Test of significance (FE)	P value
+ve	24 (100)	6 (25)	30 (62.5)	28.8	>0.001**
-ve	0 (0)	18 (75)	18 (37.5)		
Total	24 (100)	24 (100)	48 (100)		

Table 13: Combined M2-PK and Occult blood as predictors of cancer colon in relation to control group.

There was highly significant difference between Combined M2-PK and Occult blood in cancer and control groups (p>0.001).

Variable	Sensitivity	Specificity	Accuracy	PPV	NPV
Combined M2-PK and Occult blood	100%	75%	88%	80%	100%

Table 14: Validity of Combined M2-PK and Occult blood as predictors of cancer colon.

There was highly significant difference between Combined Calprotectin and Occult blood in cancer and control groups (p >0.001).

Variable	Sensitivity	Specificity	Accuracy	PPV	NPV
Combined Calprotectin and Occult blood	86%	63%	79%	72%	94%

Table 15: Validity of Combined Calprotectin and Occult blood as predictors of cancer colon.

Combined M2-PK, Calprotectin and occult blood results	Cancer colon N (%)	Control N (%)	Total	Test of significance (FE)	P value
+ve	24 (100)	9 (37.5)	33 (68.8)	21.818	>0.001**
-ve	0 (0)	15 (62.5)	15 (31.3)		
Total	24 (100)	24 (100)	48 (100)		

Table 16: Combined M2-PK, Calprotectin and occult blood as predictors of cancer colon in relation to control group.

FE: Fischer exact test.

There was highly significant difference between Combined M2-PK, Calprotectin and occult blood in cancer and control groups (p >0.001).

Variable	Sensitivity	Specificity	Accuracy	PPV	NPV
Combined M2-PK, Calprotectin and occult blood	100%	63%	81%	73%	100%

Table 17: Validity of Combined M2-PK, Calprotectin and occult blood as predictors of cancer colon.

Discussion

In the present study mean age in this study is 50 years. Cancer colon was higher among old age and males as shown in table (1) and this agrees with the Mary C. White., *et al* [1] who concluded that the risk of receiving a diagnosis of different types of cancer varies throughout a person's life span. The cumulative risk for all cancers combined increases with age. In the present study the Laboratory investigations there was a highly significant difference between studied groups regarding Hb, CRP and ESR, lowest Hb level was detected in cancer group (8.7 ± 1.7). On the other hands highest CRP and ESR levels were in cancer group (7.29 ± 4.47) and (14.71 ± 6.19) respectively. There was a significant difference between studied groups regarding platelets, lowest platelet number was detected in cancer group, there was non-significant difference between studied groups regarding WBCs, and highest WBCs number was detected in cancer group (8.05 ± 2.3) as shown in table (2) this is in agreement with Morikawa., *et al*. [2] who concluded that the FIT relies on the antibodies that bind to the globin, the decomposition of the Hb influences the tool's detection ability, and it is possible that bleeding from proximal colon may lead to an underestimation of the Hb level. Also this agrees with Jessica Watson., *et al*. [3] who declared that Cancer risk is greater with higher inflammatory marker levels, with older age and in men; risk rises further when a repeat test is abnormal but falls if it normalizes. Men over 50 and women over 60 with raised inflammatory markers have a cancer risk which exceeds the 3% NICE threshold for urgent inves-

tigation. Sensitivities for cancer were 46.1% for CRP, 43.6% ESR and 49.7% for PV. In the present study the colonoscopy showed a highly significant difference between studied groups as colonoscopy showed that 91.7% of cancer colon lesions were masses, while 62.5% of pre-cancerous colonic lesions were polyps, as shown as in table (3) this agrees with Winawer., *et al*.[4] who concluded that colonoscopy has the potential to detect lesions in the entire colorectal tract both specificity and sensitivity of colonoscopy for detecting polyps and cancer are high, at list 95% for large polyps. In the present study Calprotectin as a predictor for cancer colon There was significant difference between calprotectin in cancer and control groups as shown as in tables (7) and (8). Also positive Calprotectin was higher in cancer colon group than other groups with sensitivity and specificity 71% and 75% respectively as shown in table (8) and this agrees with Connie L. Arnold., *et al*. [5] who declared that we conducted a robust systematic review and meta-analysis. The results showed that the pooled sensitivity and specificity values of FC for CRC were approximately 83% and 61%, respectively. In addition, the overall accuracy of FC for predicting CRC was 81% and also this agrees with Jesús-Miguel Herrero., *et al*. [6] who concluded that the overall sensitivity of calprotectin for colorectal cancer and adenomatous polyps was 79% compared with 43% for FOB testing, accepting that this is in a symptomatic group of patients possibly overestimating the sensitivity values of both tests. In the present study M2-PK as a predictor of cancer colon has highly significant difference between cancer and control groups as shown as table (5) and this in agreement with Virender K. Sharma., *et al*. [7] who concluded that all cancer colon patients had M2-PK level more or equal to 3.5U/ml, however 93.3% of individual control had M2-PK level less than 3.5U/ml and this difference is statistically significant (p value = 0.001 *).The cutoff value for fecal tumor M2-PK levels was 4 U/ml, as recommended by the manufacturer and other similar studies. and also this agrees with Ali Akram., *et al*. [6] who revealed that Concerning the diagnostic performance of tumor markers in differentiating the study groups, M2PK has a good diagnostic performance in differentiating CRC from both CRP and control groups. In the current study, we validated the role of M2PK as a sensitive marker for early detection of CRC in Egyptian patients. Also this is in agreement with JOHANN KARL., *et al*. [8] who concluded that Tumor M2-pyruvate kinase (M2-PK), a tumor-associated dimeric form of enzyme pyruvate kinase, is commonly elevated in colorectal cancer and several studies have found that it is always over expression in the stool of patients with colorectal cancer. In the present study Occult blood as a predictor of cancer colon There was highly significant difference between occult blood in cancer and control groups with sensitivity, specificity and positive protective value 92%,79% and 81% respectively as shown as in tables (10) this agrees with Hisham K. Dabbous., *et al*. [9] who concluded that sensitivity, specificity and positive protective value of fecal occult blood test in CRC were 76%, 85% and 41% receptivity. In the present study Combined M2-PK and Calprotectin as predictors of cancer colon. There was highly significant difference between Combined M2-PK and Calprotectin in cancer and control groups as shown in table (11) also there was highly significant difference between Combined M2-PK and Occult blood in cancer and control groups as shown in table (14). As both positive M2-Pyruvate kinase and Occult Blood were higher in cancer colon group than other groups (91.7%) as shown in table (4) and figure (1) this is in agreement with Kyung-Jae Lee., *et al*. [10] who reported that the combination with FOBT and PK-M2 may enhance the overall pick up rate for proximal cancers. However, there are cost implications associated with M2-PK for use as a screening tool. A study by Koss and colleagues in 2007 showed the cost of M2-PK test to be £13.50 per sample. This is substantially higher than the cost of FOBT (£5.00 per person). There was highly significant difference between Combined Calprotectin and Occult blood in cancer and control groups with sensitivity and specificity 86% and 63% respectively as shown in table (15). Also our study showed that Combined M2-PK, Calprotectin and occult blood as predictors of cancer colon there was highly significant difference between cancer and control groups with sensitivity and specificity 100% and 63% respectively as shown in table (17) and this is in agreement with Mariann Rutka., *et al*. [11] who concluded that the highest sensitivity and specificity were achieved by the use of combined M2PK and FOBT test in the detection of CRC. FC seems to be useful adjuvant to the investigation of patient at high risk for colorectal neoplasia.

Conclusion

We found that:

- Colorectal Cancer (CRC) increases with age and it is more common in male
- CRP and ESR increase in CRC patients
- Feacal M2PK, FC and FOBT in stool increase significantly in CRC patients.
- Sensitivity, specificity and accuracy of screening for CRC are highest in combination of feacal M2PK, occult blood in stool and FC tests.

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